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Philippines — Laboratories

1902.—No. 2.

DEPARTMENT OF THE INTERIOR.

BUREAU OF GOVERNMENT LABORATORIES.

CHEMICAL LABORATORY.

The Preparation of Benzoyl-acetyl Peroxide, and Its Use as an Intestinal Antiseptic in Cholera and Dysentery.

PRELIMINARY NOTES.

By PAUL C. FREER, M. D., Ph. D.

MANILA:
BUREAU OF PUBLIC PRINTING.
1902.

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LETTER OF TRANSMITTAL.

OFFICE OF THE SUPERINTENDENT OF LABORATORIES,
Manila, P. I., September 11, 1902.

SIR: I have the honor herewith to transmit preliminary notes on "The preparation of benzoyl-acetyl peroxide, and its use as an intestinal antiseptic in cholera and dysentery," by Paul C. Freer, M. D., Ph. D., Superintendent of Government Laboratories.

I am, very respectfully,

PAUL C. FREER,
Superintendent of Government Laboratories.

Hon. DEAN C. WORCESTER,
Secretary of the Interior, Manila, P. I.

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THE PREPARATION OF BENZOYL-ACETYL PEROXIDE AND ITS USE AS AN INTESTINAL ANTISEPTIC IN CHOLERA AND DYSENTERY.

PRELIMINARY NOTES.

By Paul C. Freer, M. D., Ph. D.

In a paper recently published in the American Chemical Journal,[1] by Paul C. Freer and Frederick G. Novy, it was shown that the formation of organic peroxides by means of the oxygen of the air depended largely upon the surface upon which the organic materials were exposed, and in the course of the article referred to, a means was discovered of preparing benzoyl-acetyl peroxide in any desired quantity and chemically pure.

Bacteriological investigation with the solutions of this peroxide in water have shown it to be intensely active as a germicide. One part of the hydrolyzed substance to 1?? of water, and containing only 0.05 per cent of active oxygen, destroys all germs, including spores, almost instantly, and even at a dilution of 1 to 3,000 vegetating germs, as a rule, are killed within one minute, but the spores require an appreciable time. On comparing these results with similar ones with hydrogen peroxide 1 to 1,000 and phenol 5 per cent, it was shown that hydrogen peroxide, although it contained ten times as much active oxygen as the solution of benzoyl-acetyl peroxide, was by no means as effective, and the same may be said of phenol.

Experiments conducted in this laboratory demonstrated that solutions of benzoyl-acetyl peroxide as dilute as 1 part in 10,000 absolutely destroy the comma bacillus when it is placed in them in fairly large quantities on the loop of a platinum wire, and growth was inhibited, or at least extremely slow, when the dilution was

[1] American Chemical Journal, vol. 27, p. 163.

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1 to 30,000. Where a culture of beef bouillon was directly mixed with equal parts of benzoyl-acetyl peroxide solution 1 to 1,000, the growth was prevented, but at greater dilution, where large masses of beef bullion were present, the results were not so satisfactory.

Freer and Novy, at Ann Arbor, have demonstrated that large doses of benzoyl-acetyl peroxide, given in capsule form and amounting to as much as 1 gram a day for dogs weighing from 8 to 10 kilograms, were absolutely harmless, the dogs living in perfect health for from six to eight weeks, when the doses were discontinued. Mr. Charles L. Bliss demonstrated that all of the peroxide was excreted in the form of hippuric acid. Post-mortem examination of the dogs showed only a slight fatty degeneration of the liver, which might be due to the benzoyl-acetyl peroxide, but which could also very properly be owing to the abnormal conditions under which the dogs were living. Certainly the doses were far in excess of those which would be given to human beings. It has therefore been demonstrated that benzoyl-acetyl peroxide can be successfully given internally without damage, and therefore, theoretically, it should be of the greatest value as an intestinal antiseptic.

CHEMICAL STRUCTURE OF BENZOYL-ACETYL PEROXIDE.

Chemically considered, benzoyl-acetyl peroxide may be regarded as hydrogen peroxide in which one-half of the hydrogen has been substituted by the benzoyl group and the other half by acetyl. It can therefore be considered as the benzoylester of aceto-peracid or as the acetylester of benzo-peracid, and as such it is subject to hydrolysis or saponification. Experiments carried on by Freer and Novy demonstrated that benzoyl-acetyl peroxide is in itself inert and that its activity as an oxidizing substance and as a germicide only appears after it has been subjected to hydrolysis by means of water. When the substance is hydrolyzed, the reaction consists in the formation of aceto-peracid, which remains in solution, and dibenzoyl peroxide, which is precipitated as a crystalline, insoluble powder and which can be filtered from the clear solution. The germicidal effect of the solution, therefore, depends upon the presence of aceto-peracid, together with small quantities of benzo-peracid.

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In giving capsules of solid benzoyl-acetyl peroxide, this same hydrolysis will take place in the intestines and the resulting germicidal aceto-peracid will have its local effect. Dibenzoyl peroxide has been proven to be practically inert, probably owing to the great difficulty with which it is hydrolyzed.

PREPARATION OF BENZOYL-ACETYL PEROXIDE.

An attempt having been made to obtain a shipment of benzoyl-acetyl-peroxide in good condition from America, and having resulted in failure, it was clear that, if any quantity of the peroxide was to be used in the Philippine Islands, the same would necessarily have to be made on the spot, and as a consequence, a shipment of 10 kilos each of benzaldehyde and acetic anhydride was obtained from Germany.

Some fear was entertained as to the possibility of obtaining any yield of peroxide in a tropical climate, because of the continued high temperature, and consequently experiments in the preparation were at first conducted on a small scale. It soon became apparent that oxidation took place more rapidly at room temperatures common in Manila than it did in the United States, so that, whereas complete reaction was accomplished in America in three or four days, the same result could be obtained here in forty-eight hours. The yield is, however, somewhat impaired, as a larger proportion of dibenzoyl peroxide appears to be produced in this climate than is the case in America, but, nevertheless, the results were sufficiently satisfactory to warrant the construction of a larger apparatus in which 3 kilos at a time could be worked up by means of a forced current of air.

After complete oxidation, the crude product is placed in large tubulated containers, covered with petroleum ether and allowed to stand overnight, by which means the larger portion goes into solution. The extracted peroxide and solvent are then tapped off at the bottom, fresh liquid added, and the operation repeated a second time. The united solutions are then carefully concentrated on a water bath (the temperature of which must not be above 80°) until about one-third has been distilled off, after which the containers are placed in the cold room of the Ice Plant. Crystals of benzoyl-acetyl peroxide, contaminated with some dibenzoyl peroxide, gradually separate and are eventually filtered and dried. During

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the first few weeks these were used without further recrystallization. Subsequently it was shown that the impurity of dibenzoyl peroxide was present in quantites sufficient to materially reduce the doses of benzoyl-acetyl peroxide, and consequently recrystallization from petroleum ether was resorted to in all the preparations used in the later work.

In all, 2,750 grams of benzoyl-acetyl peroxide was obtained. The hospitals were at first supplied with double gelatine capsules containing 0.3 gram of benzoyl-acetyl-peroxide each, but later it was found expedient to substitute a somewhat smaller dose of 0.25 gram, to be given more frequently, the best results being finally obtained by the use of the latter, after coating with two layers of celloidin. At the same time solutions of 1 to 1,000 benzoyl-acetyl peroxide were prepared and supplied in quantity as needed, the total amount used being 1,350 liters. These solutions can be kept without deterioration for several weeks. This work was in the charge of Dr. P. L. Sherman, who kept an adequate supply on hand at all times.

TREATMENT OF CHOLERA BY BENZOYL-ACETYL PEROXIDE AND RESULTS TO SEPTEMBER 1.

The patient, on arrival at the hospital, was immediately put to bed and hot-water bags were placed over the abdomen and at the extremities. In the beginning, benzoyl-acetyl peroxide was used only in solution of 1 to 1,000, which was given by mouth as frequently as possible, and by high rectal injections every six hours, while stimulation by means of 0.006 of strychnia and 15 c. c. of brandy hypodermically was resorted to as often as demanded by the condition of the patient. If he was seen early in the disease and had considerable pain, while his general condition was good, 0.008 of morphine was given hypodermically, and if this did not relieve him, the dose was repeated in twenty or thirty minutes. Turpentine stupes and hot-water bags were also used to relieve the pain. Vomiting was generally stopped by small doses of cocaine and by pieces of cracked ice.

The preliminary experiments, conducted in a small emergency hospital in the Farola District, proved sufficiently encouraging to cause a more extended use in the hospital which was soon established at San Lazaro, and in this place the administration of double

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capsules containing each 0.25 gram of crystalline benzoyl-acetyl peroxide was first resorted to. The treatment then divided itself into two methods:

First. The administration of benzoyl-acetyl peroxide in solution and in capsules as an intestinal antiseptic for the destruction of the bacilli; and

Second. The administration of stimulants to enable the patient to survive, if possible, the effect of the toxine already present.

It was found that the patient soon tired of the solution when given by mouth, and, if its administration was persisted in, it finally produced protracted vomiting in some cases. The administration of the solution per oram was therefore discontinued and it was eventually used by rectal injection only. The double capsules were always given on an empty stomach, one every four hours, as when given on a full one they were likely to produce vomiting. High rectal injections of 1 to 1,000 solution were given every four hours during the acute stage of the disease, unless the patient was very weak. If the latter was the case and if he fought against the injection, it was not deemed safe to disturb him. The high rectal injections ferm a very important part of the treatment, especially in the second stage, where the bowel movements are approximately few, because the colon contains a large amount of toxine which is flushed out by this means. In a great many cases, where the patient was complaining of violent cramps in the abdomen, the injections seemed to give relief, so much so that a number begged for their administration. This relief was largely the result of mechanical action from the sudden dilation of the large intestine, but as careful observation has shown in subsequent hospital experience, benzoyl-acetyl peroxide also has a stimulating effect.

The patients in this hospital were mostly natives and Chinese, and of the lowest type of the inhabitants living in the Islands. They had a great dread of the Detention Camp, of disinfection, and of the destruction of their property; as a consequence, they made every effort to conceal the cases from the sanitary inspectors. Therefore, the greater number of the patients received during this stage of the epidemic had been sick during one to three days and were in a marked state of collapse. Furthermore, the natives and Chinese were unwilling to take medicine of any kind; in many

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cases great persistence on the part of the nurses was necessary before the capsules were taken, so that the excitement engendered was very deleterious. The road to the hospital was rough and at a distance from many parts of the city; therefore, the length of the trip was also a factor in the condition of the patients. These circumstances probably increased the mortality by at least 15 per cent. Of the six Americans admitted, four recovered and only two died, both of the latter giving a history of being excessive users of alcoholic beverages. One was admitted after a recent debauch. The belief that the mortality among the natives was increased by the factors mentioned above is based upon the percentage of recoveries among the Americans in this hospital.

The results of the treatment in this hospital are shown in the following table:

Schedule showing total cases treated from April 2, 1902, together with deaths and percentages from 1 year, 1–12 years, 12–21 years, 21–40 years, and over 40 years, at 3, 6, 9, 12, 18, and over 18 hours after admission.

SAN LAZARO CHOLERA HOSPITAL.

	Deaths under 1 year.		Deaths 1–12 years.		Deaths 12–21 years.		Deaths 21–40 years.		Deaths over 40 years.		Total deaths.	
	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
Under 3 hours			1	5			10	18.52	2	8	13	10.83
3–6 hours	1	100	2	10			5	9.26	6	24	14	11.66
6–9 hours			1	5	2	10	3	5.55	4	16	10	8.34
9–12 hours			3	15	2	10	4	7.41	2	8	11	9.17
12–18 hours							6	11.11			6	5.00
Over 18 hours			6	30	5	25	14	25.93	5	20	30	25.00
Total deaths	1		13		9		42		19		84	
Total per cent		100		65		45		77.78		76		[1] 70.00

[1] Average.

Total cases treated:

Under 1 year	1
1–12 years	20
12–21 years	20
21–40 years	54
Over 40 years	25
Total	120

Following the method in vogue in epidemics in India, the mortality percentage is calculated upon deaths taking place six hours and more after admission; those dying before the expiration of six hours, being in a moribund condition upon entering, are consequently not subjects for treatment. The mortality of patients dying after six hours in this hospital was 47.51, the total

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number of patients received being 120. Treatment with benzoyl-acetyl peroxide was used exclusively after the expiration of the first five days. The total mortality in this hospital, including all patients admitted, whether the deaths occurred over or under six hours, was 70 per cent, whereas, at that time, the total cholera mortality in the city was above 78 per cent.

The hospital, during the time in which benzoyl-acetyl peroxide was used, was in charge of Dr. James W. Jobling, to whose untiring efforts and continued attention much of the success was due, Dr. Jobling being ably assisted by Dr. T. K. Hunt.

In the first part of April it became evident that the San Lazaro Hospital was becoming infected, it being in tents, and in a more or less exposed locality, and the Board of Health decided to establish a new tent hospital at Santa Mesa. This was opened on April 12, and both the detention camp and hospital were finally placed in charge of Dr. Thos. R. Marshall, whose earnest work deserves the highest commendation. The records of treatment show that three methods were adopted:

First. Benzoyl-acetyl peroxide.

Second. Benzoyl-acetyl peroxide mixed with other remedies; and

Third. Remedies other than benzoyl-acetyl peroxide.

The results are as follows:

The number of patients treated in the Santa Mesa Cholera Hospital from April 12 until May 5, inclusive, was 186, of which 152 died and 34 were discharged, cured. The condition of the patients was much the same as in San Lazaro, the long trip and duration of sickness before admission being deleterious. In this institution only a certain percentage of cases was treated with benzoyl-acetyl peroxide solution and capsules, other measures being used with the balance, the three classes being kept separate. The doctors in charge reported irritation of the stomach as being produced by the capsules, which did not appear to be the case with the patients treated at San Lazaro.

"The introduction of the drug along the intestinal canal was the end desired. The administration of the powder, by mouth in single capsules, soon gave place to the use of double capsules, and this was maintained as routine treatment, in doses from 0.20 to 0.32 gram every two to four hours. Gastric irritation was a common symptom presented and drugs directed to meet this indication were continually employed. It was observed very early that benzoyl-acetyl-peroxide was best retained on an empty stomach,

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for when given on a full stomach, retching and frequently vomiting occurred. This prevalency of periodic gastric intolerance, to anything foreign, greatly interfered with the proper and regular administration of the drug in this hospital."[1]

This effect was subsequently avoided in Santiago Hospital (established on May 5), when the method of coating the capsules with two layers of celloidin was adopted. It is difficult to explain why the patients of the Santa Mesa Hospital only, suffered from marked gastric irritation after taking the drug. Perhaps the cause of this is to be found in the fact that the benzoyl-acetyl peroxide was delivered at a great distance from the laboratories and therefore probably melted in the capsules, after which the action of the air and the heat of the sun facilitated hydrolysis, which, once inaugurated, would continue rapidly if the hyperoxide was kept in contact with the moisture and imperfectly cooled. The absorption of water through the coating of the capsules and the consequent hydrolysis would produce aceto-peracid, which is irritating, and the effects of which would become apparent in the stomach. Coating with celloidin and preserving in pasteboard boxes, covered with oiled paper, avoids this difficulty. Despite these obstacles, the statistics of this hospital demonstrate that the best results were obtained with the benzoyl-acetyl peroxide treatment. This becomes apparent by the study of the following table:

Total number of cases	186
Total death rate, per cent	81.7
Total death rate of patients living over six hours, per cent	48.9
Total death rate of patients living under six hours, per cent	28.4
Died before arriving, per cent	4.3

Of these patients, 93 received benzoyl-acetyl peroxide treatment, either by rectal injections, by capsule, or both, together with cardiac stimulants, hot applications, enemas of normal salt solution, or saline transfusion; 29 received other treatments, and 17 a mixed treatment, using benzoyl-acetyl peroxide only as enemas; 8 no treatment at all, and of 39 there is no record. Of the 93 cases treated with benzoyl-acetyl peroxide, 26 recovered; of those who received benzoyl-acetyl peroxide mixed with other remedies, 7 recovered, and of the 29 patients not receiving benzoyl-acetyl peroxide none recovered. The benzoyl-acetyl peroxide treatment, therefore, has a total death rate of 72 per cent as against a death rate of 100

[1] Report of Dr. T. R. Marshall.

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per cent for treatments which contained no benzoyl-acetyl peroxide. The fact must be taken into consideration, however, in this connection, that a number of the cases not receiving benzoyl-acetyl peroxide treatment were practically moribund at the time of admission, so that the death rate of 41.1 is recorded for these patients under six hours. The above comparison does not of necessity represent the germicidal value of the drug, because stimulation, heat, diet, nursing, etc., have no credit in the statistics for the good they probably rendered, but some conclusions can be drawn from the death rate of those patients receiving no benzoyl-acetyl peroxide.

The treatment resorted to in this hospital consisted, quoting from the report of Dr. Marshall, "in giving 1 to 1,000 solution by mouth and rectal injection. By mouth it was soon discontinued, due to gastric intolerance, but by rectal injections beneficial results were evident. This was soon increased in efficiency by the addition of normal salt solution to an equal quantity of 1 to 1,000 solution of benzoyl-acetyl-peroxide, which finally became a routine treatment. Of the treatments where the benzoyl-acetyl-peroxide was used, it was not the only factor, the patient being given enemas, strychnine, hot applications, and whisky or brandy, in some cases small doses of caffein being used."

The records of the first few days of this hospital were unfortunately not complete, so that absolutely definite conclusions as to the value of the various treatments can not be reached from this report only.

The hospital at Santa Mesa, being in a situation far removed from the city, was finally abandoned, and on May 5 the Board of Health secured ample quarters in the Santiago Hospital, where facilities for treating patients were much superior to those which were previously available and where a systematic comparative treatment could be inaugurated. The Santiago Hospital was in the able hands of Dr. E. A. Southall during the first month; subsequently, after his illness, Dr. Lindley took charge. Both gentlemen worked with the greatest zeal, and developed a number of new features of treatment.[1] In this they were assisted by Dr. Jobling, who acted as bacteriologist. As a result of experience, they finally

[1] The results and statistics from the Santiago Hospital are taken from reports by Drs. Southall and Lindley. Dr. Southall covered the period up to June 17, and Dr. Lindley the remainder, including the statistics.

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developed the following practice: When a patient was not in a moribund condition as a result of the violent toxæmia produced by cholera, but was in the second stage, or state of collapse, it became the practice among the attending physicians to resort to subcutaneous injections of normal salt solution, one-half liter, combined with a like amount of benzoyl-acetyl peroxide solution of 1 to 1,000. The point selected for the injection was usually the breast. It was observed that the stimulating effects of the normal salt solution combined with the benzoyl-acetyl peroxide was more direct and lasting than that of the normal salt alone, the combination acting as a decided stimulant upon the circulatory system, increasing the volume and force of the blood current. The drug appeared to act as a stimulant upon the respiratory system and no marked effects were noted upon the nervous system.

Capsules, double-coated with celloidin and containing each 0.1666 gram of benzoyl-acetyl peroxide, were found to pass through the small intestine undissolved and were in some instances recovered from the feces, having lost about 0.1333 gram of the drug during their passage, and thus by osmosis the hyperoxide was gradually distributed along the length of the intestinal canal. High rectal enemas of benzoyl-acetyl peroxide 1 to 2,000 were given in a large proportion of the cases and no ill effects were noted from this method of administration excepting a nervous excitement incident to the passage of the tube, in a few cases.

In 2½ per cent of the cases of cholera treated in this hospital evidence of intestinal hemorrhages were seen at the time of admission, the blood passed being usually slight in amount, and it was not observed that the benzoyl-acetyl peroxide in any way influenced the amount or gross appearance of the hemorrhagic stools, save by the possible action of flushing out the large bowel and rectum. This lavage of the large bowel was in many instances followed by decided relief from pain and a diminution of restlessness and semidelirium, this having also been observed in the previous hospital at San Lazaro.

The use of alcohol as a stimulant was discontinued in many instances in this hospital, as the mental, physical, and emotional excitement was followed by a grave reaction incident to its use. A careful administration of strychnine was prescribed in most cases of collapse, accompanied by the use of hot-water bags, hot-

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water bottles, etc., atropine being used to give relief in cases of sudden collapse. Alcoholic baths were administered where indicated, and enemas of benzoyl-acetyl peroxide mixed with normal salt at 44° to 44.5° C. were also employed. Alcoholic stimulants in the form of sherry and malaga wine were only resorted to at the time of convalescence.

The only other treatment used by American physicians, as the table will show, which can come into consideration in addition to benzoyl-acetyl peroxide alone, is the one with guiacol carbonate and calomel mixed with the peroxide. The guiacol carbonate and calomel was administered in doses of one-tenth grain of calomel to 3 grains of guiacol carbonate in powder, every four to six hours, and it markedly lessened the bowel movements. The drug had very little effect upon the circulatory, respiratory, and nervous systems, with the exception, perhaps, of a slight reduction of temperature in some instances. A much larger percentage of cases treated by other methods died, so that the American physicians in attendance finally decided in favor of using benzoyl-acetyl peroxide. The treatment with this substance, as outlined above, is now exclusively used with American patients, but the native physicians, who have been in charge of the Filipino wards for the past few weeks, have not, as yet, attempted to use it, but have confined themselves to other methods.

The guiacol carbonate and calomel treatment alone was used up to the date of writing in 54 cases and shows a percentage of recoveries of 14.18; against this, benzoyl-acetyl peroxide, mixed with guiacol carbonate and calomel had a total recovery of 41.94 per cent, and benzoyl-acetyl-peroxide alone of 40.42 per cent. These tables would show a slight advantage in favor of the mixed treatment, but the death rate for the latter, under six hours, of only 4.49 per cent, as against 16.31 per cent for benzoyl-acetyl-peroxide, goes to show that in the latter stages of the epidemic, when many less severe cases were encountered, the mixed treatment had the advantage, because the patients were in a better condition on entering the hospital. This will be understood when it is remembered that the treatment with benzoyl-acetyl-peroxide was inaugurated at the beginning, when the most adverse conditions as to mortality were encountered. The average death rate in the city during June was 86.2 per cent. The mixed treatment was only tried later, when

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the death rate had sunk to 70 per cent, and would thus gain an advantage in the conditions in which the patients reached the hospital. If this circumstance is considered, it is evident that benzoyl-acetyl peroxide alone is at least of the same value as the peroxide mixed with guiacol carbonate and calomel, although the latter apparently does little harm. In this connection it is worthy of note, however, that the percentage of deaths over six hours is only 43.25 for benzoyl-acetyl peroxide, as against 53.55 for the mixed treatment. When we consider that patients who die under six hours can scarcely be regarded as having received treatment at all, it is evident that the advantage lies with benzoyl-acetyl peroxide alone. The majority of the patients in this hospital were not treated by either of the above methods. Four hundred and eight cases were treated with either benzoyl-acetyl peroxide or benzoyl-acetyl peroxide mixed with guiacol carbonate and calomel, and of these 169 recovered; 593 received other treatment, and of these 106 only recovered.

The following gives a summary of results:

Total cases received	1,031
Cases in hospital	30
Reported upon	1,001

Benzoyl-acetyl peroxide treatment.	No.	Per cent.
Total cases treated	141	
Deaths under 6 hours	23	16.31
Deaths over 6 hours	61	43.25
Recoveries	57	40.42

Benzoyl-acetyl peroxide mixed with guiacol carbonate and calomel.	No.	Per cent.
Total cases treated	267	
Deaths under 6 hours	12	4.49
Deaths over 6 hours	143	53.55
Recoveries	112	41.94

Guiacol carbonate and calomel treatment.	No.	Per cent.
Total cases treated	54	
Deaths under 6 hours	16	29.62
Deaths over 6 hours	30	55.55
Recoveries	8	14.81

	No.	Per cent.
Total cases treated	1,001	
Deaths	696	69.53
Recoveries	305	30.46

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On July 21 certain wards were turned over to native physicians and nurses, who inaugurated treatments which had proven efficacious in the previous cholera epidemic in Manila. These methods have varied considerably from time to time and, as individual physicians adopted different remedies, details as to the exact measures employed in a given series can not be given. The treatment practically divided itself into two heads; one with saline enemas three times a day and administration of calomel 3 centigrams, tannalbin and bismuth 25 milligrams every three hours, and the second class with tannic acid enemas 1 to 100, calomel and benzonaphthol every three hours. As stimulants, hypodermic injections of strychnine, sodium benzoate, caffein citrate, and subcutaneous injections of sodium benzoate and caffein citrate combined with one-third normal salt solution were used. The following tables, covering the period between July 21 and September 1, are appended:

Cases treated by American physicians between July 21 and September 1, 1902.

	No.	Per cent.
Total cases treated	138	
Deaths under 6 hours	17	12.31
Deaths over 6 hours	60	43.48
Recoveries	61	44.20

Cases treated by native physicians between July 21 and September 1, 1902.

	No.	Per cent.
Total cases treated	136	
Deaths under 6 hours	31	22.80
Deaths over 6 hours	56	41.19
Recoveries	49	36.02

As will be seen from the above, the native physicians have a very favorable percentage of recoveries, but the total is nevertheless 8.18 per cent of all cases less than that to be ascribed to methods using benzoyl-acetyl peroxide.

Five hundred and three cases are not recorded in any of the above treatments. These can not be classified, as the means employed and remedies administered varied with individual physicians and at different times, many of these cases representing the class of

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patients who were brought into the hospital in a moribund condition and who received no treatment at all. None of them received benzoyl-acetyl peroxide. The percentage of recoveries with this remainder was 14.3. The total percentage of recoveries for the entire hospital was 30.46.

BENZOYL-ACETYL-PEROXIDE IN AMEBIC DYSENTERY

Benzoyl-acetyl peroxide has given very satisfactory results in amebic dysentery. In the treatment of this disease one should recall that not one, but two, factors are concerned in the etiology of the malady, and particularly in its progress. These factors are the amoebæ and the intestinal bacteria, both of which must be attacked. In the following, Dr. R. P. Strong, of the Biological Laboratory, reports the results obtained with eleven cases:

It has been demonstrated in the Biological Laboratory by experimental studies on cats that the bacteria in the intestine, always present, and other varieties of micro-organisms, occasionally present, may play an important part in the extension of the lesions in amebic dysentery, and that it is particularly to their influence that the necroses found in the intestine in this disease are due. Bacteria are always plentiful in the sections from experimental dysenteric cases and in very large numbers in the necrotic areas. The same is true in sections of the intestine in human dysenteric cases. While it seems not unlikely that the amoebæ proceed in advance of the bacteria and make openings for them in the mucosa, the latter, however, closely follow them, modify the lesions, and cause increased tissue destruction. Particularly is this true when the pyogenic cocci are present in large numbers, and indeed the immediate cause of death in the disease may be due to these micro-organisms.

Quinine used in enemata has hitherto usually given the best results in the treatment of amebic dysentery. The advantages of benzoyl-acetyl peroxide over quinine, however, are apparent, for the latter, while quite capable of killing amoebæ even in dilute solutions, also attacks the bacteria which are present in the intestines, and it has been found possible by its use to greatly reduce the number of micro-organisms in the stools.

Benzoyl-acetyl peroxide is therefore now used for the routine treatment of this disease in the following manner:

The patients take daily, or in some cases oftener, a 1 to 1,000

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